# PATENT COOPERATION TREATY



# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| CLJ/B45326 | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/EP 03/12160 | 30.10.2003 | 01.11.2002 |
| International Patent Classification (IPC) or both national classification and IPC | | |
| A61K39/13 | | |
| Applicant | | |
| GLAXOSMITHKLINE BIOLOGICALS S.A. et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 13.05.2004 | 26.11.2004 |
| Name and mailing address of the international preliminary examining authority: | Authorized Officer |
| European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Pilling, S<br>Telephone No. +49 89 2399-8461 |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/12160

## I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

**Description, Pages**

1-51 as originally filed

**Claims, Numbers**

1-32 received on 05.11.2004 with letter of 04.11.2004

**Drawings, Sheets**

1/3-3/3 as originally filed

2. With regard to the **language,** all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-32 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | 1-32 |
| | No: | Claims | |
| Industrial applicability (IA) | Yes: | Claims | 1-32 |
| | No: | Claims | |

2. Citations and explanations

   **see separate sheet**

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D12 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

2. The relevant disclosures of the aforementioned compositions are summarised as follows;

Document D1 discloses the production of foamed glass matrices comprising oral polio virus in combination with a stabilising agent, *i.e.* trehalose/HSA, lactitol/HSA or trehalose/sorbitol/HSA (see page 3 lines 12 to 16 and Example 5c)

Document D2 disclosed coating of sugar candy kernels with an aqueous suspension of poliovirus followed by drying (see page 1 column 1 line 42 to column 2 line 49 and Example 1)

Document D3 describes the production of stable dry formulations of polio virus by drying the virus in the presence of trehalose (see column 2 lines 1 to 13 and Example 3)

Document D4 describes the formulation of poliovirus in a hydrophilic acrylate or methacrylate ester (see column 1 lines 20 to 35, column 7 line 53 to column 8 line 34, Example 2, 9, 11 and Claim 1)

Document D5 discloses the production of a dried stable immunogen for oral administration using a gelatin stabiliser and indicates that the immunogen can be attenuated live polio virus (see column 1 lines 45 to 56 and column 2 lines 33 to 39)

Document D6 discloses the production of a further dried stable immunogen for oral administration using a fatty acid ester of sucrose as a stabiliser and indicates that the immunogen can be attenuated polio virus (see page 2 line 57 to page 3 line 9)

Document D7 describes the production of a peroral vaccine powder comprising an

immunogen and a polyol stabiliser. The immunogen may be inactivated/ attenuated virus including polio.

Documents D8 and D9 each disclose further stabilised-lyophilized polio vaccines.

Claims 1 to 32: immunogenic compositions/ kits/ vaccines, methods of making vaccines and methods of preserving compositions

3. Documents D1 to D9 each disclose dried vaccine compositions comprising inactivated polio virus (IPV) together with a stabilising agent for reconstitution in an aqueous solution (see the summary of the disclosure of these documents above). There is no suggestion or teaching in these documents, however, towards the use of a bacterial polysaccharide or oligosaccharide as a stabilising agent.

4. It is further noted that the Applicant has provided evidence (see for Example present Example 6) that the use of bacterial polysaccharide/oligosaccharide as a vaccine stabilising agent leads to improved retention of IPV antigenicity in comparison with at least one commonly used vaccine stabilising agent, *i.e.* sucrose. This effect does not appear to have been predictable from any of the presently available prior art documents. Thus, it appears that the presently claimed subject matter makes an inventive contribution to the present art.

5. Thus, the subject matter of Claims 1 to 32 appears to be new and inventive (Article 33(2) and 33(3) PCT).

**Claims as amended**

1. An immunogenic composition comprising IPV, a bacterial polysaccharide or oligosaccharide and a stabilising agent, all formulated as a dried composition, which after reconstitution, is capable of generating an immune response against polio virus.

2. The immunogenic composition of claim 1 comprising a capsular polysaccharide or oligosaccharide antigen from *Haemophilus influenzae* b (Hib).

3. The immunogenic composition of claim 1 or 2 wherein the polysaccharide or oligosaccharide is conjugated to a carrier protein.

4. The immunogenic composition of claim 3 wherein the polysaccharide or oligosaccharide is conjugated to tetanus toxoid.

5. The immunogenic composition of claim 2-4 wherein the polysaccharide or oligosaccharide is adsorbed onto aluminium phosphate.

6. The immunogenic composition of claim 1-5 comprising a capsular polysaccharide or oligosaccharide derived from *N. meningitidis* C.

7. The immunogenic composition of claim 1-6 additionally comprising a capsular polysaccharide or oligosaccharide derived from any of *N. meningitidis* A, Y or W or combination thereof.

8. The immunogenic composition of claim 6-7 wherein the meningococcal polysaccharides or oligosaccharides are conjugated to a carrier protein.

9. The immunogenic composition of claim 8 comprising a Hib polysaccharide or oligosaccharide and at least one meningococcal polysaccharide or oligosaccharide conjugated to the same type of carrier protein.

10. The immunogenic composition of claim 8 comprising a Hib polysaccharide or oligosaccharide and at least one meningococcal polysaccharide or oligosaccharide conjugated to different carrier proteins.

11. The immunogenic composition of claim 1-10 further comprising phenol red.

12. The immunogenic composition of claim 1-11 wherein the dried composition is freeze dried.

13. The immunogenic composition of claim 1-12 wherein the dried composition is a foamed glass.

14. The immunogenic composition of claims 1-11 wherein the dried composition is a highly viscous liquid.

15. The immunogenic composition of claim 14 wherein the highly viscous liquid has not been frozen.

16. A method of making a vaccine comprising the step of reconstituting the immunogenic composition of claims 1-15 in an aqueous solution.

17. The method of claim 16 wherein the aqueous solution comprises Diphtheria toxoid, Tetanus toxoid and Pertussis antigens (acellular or whole cell).

18. The method of claim 17 where the DTP vaccine is at least in part adjuvanted with aluminium hydroxide.

19. The method of claim 17 or 18 wherein the aqueous solution comprises Hepatitis B surface antigen.

20. A kit comprising the immunogenic composition of claims 1-15 in one container and liquid DTP (acellular or whole cell) vaccine in a second container.

21. The kit of claim 20 further comprising Hepatitis B surface antigen in the second container.

22. A vaccine comprising the immunogenic compositions of claims 1-15.

23. The vaccine of claim 22 which is reconstituted into an aqueous solution prior to use.

24. A container with a water repellent internal surface containing the vaccine of claim 22-23.

25. A method of preserving a composition comprising IPV, a bacterial polysaccharide or oligosaccharide and a stabilising agent comprising the steps of:

a) preparing a preservation sample by suspending or dissolving IPV and a bacterial polysaccharide or oligosaccharide in a solution of a stabilising agent;
b) subjecting the preservation sample to such temperature and pressure conditions that solvent is lost from the preservation sample ; and
c) removing solvent until the preservation sample dries to form a solid or highly viscous liquid in which the antigenicity of IPV is retained.

26. The method of claim 25 wherein the preservation sample is dried in a container with a water repellent interior surface.

27. The method of claim 25 or 26 wherein the preservation sample bubbles to form a foam during step b).

28. The method of claim 27, wherein the sample is at least partially frozen before commencing the drying process.

29. The method of claim 27 wherein the preservation sample becomes at least partially frozen during step b).

30. The method of claim 25 wherein, during step b) the preservation sample is subjected to such temperature and pressure conditions so that the preservation sample looses solvent by evaporation, without freezing or bubbling involved in foam formation, to form a viscous liquid and during step c) solvent is removed until the preservation sample dries to form a highly viscous liquid.

31. The method of claim 26-30 wherein the preservation sample comprises Hib polysaccharide or oligosaccharide.

32. The method of claim 26- 31 wherein the preservation sample comprises, polysaccharide or oligosaccharide derived from any of *N. meningitidis* A, C, Y or W or combination thereof.